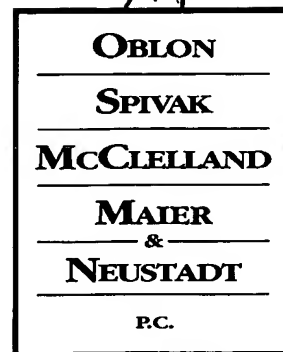




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RE: Application Serial No.: 10/631,351

Applicants: Oliver HARNACK et al

Filing Date: July 31, 2003

For: METHOD OF ATTACHING HYDROPHILIC
SPECIES TO HYDROPHILIC MACROMOLECULES
AND IMMOBILIZING THE HYDROPHILIC
MACROMOLECULES ON A HYDROPHOBIC
SURFACE

Group Art Unit: 1641

Examiner: YU, MELANIE J.

SIR:

Attached hereto for filing are the following papers:

SUBSTITUTE APPEAL BRIEF WITH ATTACHED APPENDIX (6 PP.)
AND CITED REFERENCE (DICTIONARY EXCERPT, 4 PP.)

Our credit card payment form in the amount of \$-0- is attached covering any required fees. In the event any variance exists between the amount enclosed and the Patent Office charges for filing the above-noted documents, including any fees required under 37 C.F.R. §1.136 for any necessary Extension of Time to make the filing of the attached documents timely, please charge or credit the difference to our Deposit Account No. 15-0030. Further, if these papers are not considered timely filed, then a petition is hereby made under 37 C.F.R. §1.136 for the necessary extension of time. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :
OLIVER HARNACK, ET AL. : EXAMINER: YU, MELANIE J.
SERIAL NO: 10/631,351 :
FILED: JULY 31, 2003 : GROUP ART UNIT: 1641
FOR: METHOD OF ATTACHING :
HYDROPHILIC SPECIES TO
HYDROPHILIC MACROMOLECULES
AND IMMOBILIZING THE
HYDROPHILIC MACROMOLECULES
ON A HYDROPHOBIC SURFACE

SUBSTITUTE APPEAL BRIEF

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

Further to the July 5, 2006 Notice of Appeal, and in response to the August 22, 2006 Notification of Non-Compliant Appeal Brief, Appellants respectfully request entry and consideration of this Substitute Appeal Brief in place of the August 2, 2006 Appeal Brief. Appellants appeal from the January 4, 2006 Final Rejection in the above-captioned application.

I. REAL PARTY IN INTEREST

The real party in interest in this appeal is Sony Deutschland GMBH, Koeln, Germany.

II. RELATED APPEALS AND INTERFERENCES

Appellants, Appellants' legal representative and the assignee are aware of no appeals, interferences, or judicial proceedings which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

Claims 2-20 are pending and stand rejected.

Claims 1 and 21-23 have been cancelled.

The rejections of claims 2-20 are being appealed.

IV. STATUS OF AMENDMENTS

An Amendment After Final Rejection was filed on June 8, 2006.

In the July 5, 2006 Advisory Action, the Examiner indicated that the amendments set forth in the June 8, 2006 Amendment After Final Rejection were entered for the purposes of this appeal.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 2 is drawn to a method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface by first providing a hydrophobic surface, then changing the nature of that hydrophobic surface by immobilizing hydrophilic macromolecules on the hydrophobic surface, and finally exposing the hydrophilic macromolecules immobilized on the hydrophobic surface to hydrophilic species, whereby the hydrophilic species are attached to the hydrophilic macromolecules. *See, e.g.*, specification page 3, lines 1-8 and claim 2. Claims 3-20 depend directly or indirectly from claim 2.

VI. GROUND OF REJECTION

A. Ford and Caldwell

Claims 2-18 and 20 are rejected as obvious, 35 U.S.C. 103, over Ford (U.S. 2002/0065242) in view of Caldwell (U.S. 5,516,703).

B. Ford, Caldwell and Berning

Claim 19 is rejected as obvious, 35 U.S.C. 103, over Ford (U.S. 2002/0065242) in view of Caldwell (U.S. 5,516,703) further in view of Berning (Nuclear Medicine & Biology, 1998).

C. 812 Application and Caldwell

Claims 2-6, 11, 15 and 17-19 are provisionally rejected for obviousness-type double patenting over claims 1-5, 14 and 15 of application 10/210,812 in view of Caldwell (U.S. 5,516,703).

D. 049 Application and Caldwell

Claims 2-6, 11, 15 and 17-19 are provisionally rejected for obviousness-type double patenting over claims 1-4, 14-16 and 20 of application 09/990,049 in view of Caldwell (U.S. 5,516,703).

VII. ARGUMENT

Appellants submit that the outstanding rejections should be reversed for the following reasons. All of the rejections are premised on the Examiner's erroneous belief that Caldwell teaches the use of a hydrophobic substrate as a platform for the immobilization of hydrophilic macromolecules and, thus, all of the rejections are unsustainable.

A. Ford and Caldwell

As indicated above, claims 2-18 and 20 are rejected as obvious, 35 U.S.C. 103, over Ford (U.S. 2002/0065242) in view of Caldwell (U.S. 5,516,703).

Claim 2 recites:

A method of attaching hydrophilic species to
hydrophilic macromolecules immobilized on a hydrophobic
surface, said method comprising the steps:
(i) providing a hydrophobic surface,

- (ii) **immobilizing hydrophilic macromolecules on the hydrophobic surface,**
(iii) **exposing the hydrophilic macromolecules immobilized on the hydrophobic surface to hydrophilic species,** whereby the hydrophilic species are attached to the hydrophilic macromolecules.

In this method, hydrophilic macromolecules are immobilized **on** a hydrophobic surface.

Then, these immobilized hydrophilic macromolecules are exposed to hydrophilic species, such as nanoparticles, which attach to the immobilized hydrophilic macromolecules.¹

The Examiner asserts that Ford discloses a method including providing a surface, immobilizing hydrophilic nucleic acids on the surface, and exposing the immobilized nucleic acids to metal complexes of gold nanoparticles. *See* January 4, 2006 Final Rejection, page 3, lines 9 to 17. The Examiner concedes that Ford fails to disclose or suggest "immobilizing hydrophilic macromolecules on the hydrophobic surface," as recited in instant claim 2. *See id.*, line 17. However, the Examiner asserts that it would have been obvious to "include in the method of Ford et al., a hydrophobic surface as taught by Caldwell in order to provide a surface with a high degree of reactivity and little or no background non-specific reactivity." *See id.*, page 3, line 19 to page 4, line 2.

This assertion, and thus the rejection (as well as the other outstanding rejections), are premised on the Examiner's mistaken understanding that "Caldwell et al teach a hydrophobic

¹ While the meaning of the terms "hydrophilic" and "hydrophobic" are likely very well known to the Board, the following is from <http://www.answers.com/topic/hydrophilic> and <http://www.answers.com/topic/hydrophobic>:

HYDROPHILIC:

Meaning #1: (chemistry) having a strong affinity for water; tending to dissolve in, mix with, or be wetted by water

Antonym: hydrophobic (meaning #1)

HYDROPHOBIC

Meaning #1: (chemistry) lacking affinity for water; tending to repel and not absorb water; tending not to dissolve in or mix with or be wetted by water

Antonym: hydrophilic (meaning #1)

substrate (col. 7, lines 19-30), in order to provide a surface with specific reactivity." *See id.*, page 3, lines 18 to 19. Contrary to the Examiner's understanding, Caldwell does not use a hydrophobic surface as a working surface. Caldwell specifically teaches that it is his hydrophilicly-coated substrate, and not a hydrophobic surface, that provides higher specific reactivity and little or no background non-specific reactivity:

[T]he surfaces ***provided by the coatings of the invention*** have a ***higher specific reactivity*** per unit area of surface with an even distribution of reactivity. In addition, ***there is little or no background nonspecific reactivity resulting from adsorption to unshielded surfaces.***

See column 4, lines 22 to 26 (emphasis added). Caldwell's coatings are made of a modified polymer surfactant, which is coated onto the surface of an underlying hydrophobic substrate:

The modified polymeric surfactant is adsorbed upon a hydrophobic polymer substrate to provide a surface with specific reactivity.

See column 7, lines 18 to 20. Importantly, the result is a substrate with a hydrophilic surface:

The surface resulting from the modified polymer adsorbed on the hydrophobic substrate is hydrophilic and quite compatible with proteins that can be immobilized on the surface through the reactive sites.

See column 4, lines 4 to 7 (emphasis added). Caldwell therefore teaches that before any use is made of a hydrophobic substrate, for example by attaching proteins thereto, the nature of the hydrophobic surface must first be completely changed such that a hydrophilic surface is presented. Thus, even if one were motivated to use Caldwell's substrate with the nucleic acids of Ford the substrate used would be the *modified* substrate of Caldwell, i.e., the *hydrophilic* surface-modified substrate of Caldwell.

These facts have been pointed out to the Examiner. The Examiner responded in the July 5, 2006 Advisory Action (*see* Continuation Sheet), that "[t]he claims do not exclude

additional layers between the hydrophobic substrate and the hydrophilic macromolecules and also do not state that the hydrophilic macromolecules must be immobilized directly on the hydrophobic substrate." Again, the Examiner is wrong.

All pending claims require "immobilizing hydrophilic macromolecules **on** the hydrophobic surface" and "exposing the hydrophilic macromolecules immobilized **on** the hydrophobic surface to hydrophilic species, whereby the hydrophilic species are attached to the hydrophilic macromolecules." The common meaning of "on" is "in contact with." For Example, Webster's Collegiate Dictionary (excerpt attached hereto) defines the word "on" as meaning "a- used as a function word to indicate position in contact with and supported by the top surface of {the book is lying _ the table} b - used as a function word to indicate position in or in contact with an outer surface {the fly landed _ the ceiling}..." This common meaning is consistent with the meaning of the word "on" as used in the specification of the present application where, in Example 1 (*see* specification, pages 8-9), a SiO₂ substrate (hydrophilic) is coated with polystyrene (hydrophobic) prior to contact with ctDNA (hydrophilic macromolecules). In the present application and claims, "immobilizing hydrophilic macromolecules **on** the hydrophobic surface" means *directly* on. Put another way, there is no difference between "on" and "directly on."

In view of the foregoing, it is plain that Caldwell, like Ford, fails to disclose or suggest a method including "immobilizing hydrophilic macromolecules on the hydrophobic surface." As neither Ford nor Caldwell discloses or suggests "immobilizing hydrophilic macromolecules on the hydrophobic surface," the combination of references fails to disclose or suggest each and every feature of claim 2.

For the foregoing reasons, claim 2 would not have been rendered obvious by Ford and Caldwell. Claims 3-18 and 20 depend from claim 2 and, thus, also would not have been rendered obvious by Ford and Caldwell.

B. Ford, Caldwell and Berning

As indicated above, claim 19 is rejected as obvious, 35 U.S.C. 103, over Ford (U.S. 2002/0065242) in view of Caldwell (U.S. 5,516,703) further in view of Berning (Nuclear Medicine & Biology, 1998).

For the reasons set forth above in Section A, neither Ford nor Caldwell discloses or suggests a method including "immobilizing hydrophilic macromolecules on the hydrophobic surface," as recited in claim 2. Berning does not remedy the deficiencies of Ford and Caldwell.

The Examiner cites Berning for its alleged disclosure of tris(hydroxymethyl) phosphine-gold nanoparticles. *See* January 4, 2006 Final Rejection, page 5, lines 3 to 5. However, Berning, like Ford and Caldwell, fails to disclose or suggest a method including "immobilizing hydrophilic macromolecules on the hydrophobic surface." As none of Ford, Caldwell and Berning discloses or suggests "immobilizing hydrophilic macromolecules on the hydrophobic surface," the combination of references fails to disclose or suggest each and every feature of claim 2.

For the foregoing reasons, claim 2 would not have been rendered obvious by Ford, Caldwell and Berning. Claim 19 depends from claim 2 and, thus, also would not have been rendered obvious by Ford, Caldwell and Berning.

C. 812 Application and Caldwell

As indicated above, claims 2-6, 11, 15 and 17-19 are provisionally rejected for obviousness-type double patenting over claims 1-5, 14 and 15 of application 10/210,812 in view of Caldwell (U.S. 5,516,703).

The Examiner asserts that claims 1-5, 14 and 15 of the 812 application are directed to a hydrophilic macromolecule exposed to a hydrophilic nanospecies, the resulting complex being immobilized on a substrate. *See* January 4, 2006 Final Rejection, page 5, lines 14 to 16. The Examiner concedes that claims 1-5, 14 and 15 of the 812 application do not recite "immobilizing hydrophilic macromolecules on the hydrophobic surface," as recited in instant claim 2. *See* January 4, 2006 Final Rejection, page 5, line 17. However, the Examiner asserts that a skilled artisan would be motivated by the teachings of Caldwell to modify the subject matter of claims 1-5, 14 and 15 of the 812 application to include "immobilizing hydrophilic macromolecules on the hydrophobic surface." For the reasons set forth above in Section A, Caldwell does not disclose or suggest a method including "immobilizing hydrophilic macromolecules on the hydrophobic surface." As neither claims 1-5, 14 and 15 of the 812 application nor Caldwell discloses or suggests "immobilizing hydrophilic macromolecules on the hydrophobic surface," the combination of references fails to disclose or suggest each and every feature of instant claim 2.

For the foregoing reasons, instant claim 2 is not obvious over the claims of the 812 application and Caldwell. Instant claims 3-6, 11, 15 and 17-19 depend from instant claim 2 and, thus, also are not obvious over the claims of the 812 application and Caldwell.

D. 049 Application and Caldwell

As indicated above, claims 2-6, 11, 15 and 17-19 are provisionally rejected for obviousness-type double patenting over claims 1-4, 14-16 and 20 of application 09/990,049 in view of Caldwell (U.S. 5,516,703).

The Examiner asserts that claims 1-4, 14-16 and 20 of the 049 application are directed to a hydrophilic macromolecule exposed to a hydrophilic nanospecies, the resulting complex being immobilized on a substrate. *See* January 4, 2006 Final Rejection, page 6, lines 5 to 7. The Examiner concedes that claims 1-4, 14-16 and 20 of the 049 application do not recite "immobilizing hydrophilic macromolecules on the hydrophobic surface," as recited in instant claim 2. *See* January 4, 2006 Final Rejection, page 6, line 8. However, the Examiner asserts that a skilled artisan would be motivated by the teachings of Caldwell to modify the subject matter of claims 1-4, 14-16 and 20 of the 049 application to include "immobilizing hydrophilic macromolecules on the hydrophobic surface." For the reasons set forth above in Section A, Caldwell does not disclose or suggest a method including "immobilizing hydrophilic macromolecules on the hydrophobic surface." As neither claims 1-4, 14-16 and 20 of the 049 application nor Caldwell discloses or suggests "immobilizing hydrophilic macromolecules on the hydrophobic surface," the combination of references fails to disclose or suggest each and every feature of instant claim 2.

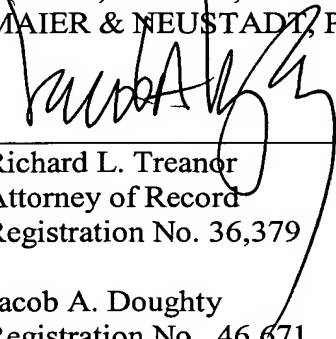
For the foregoing reasons, instant claim 2 is not obvious over the claims of the 049 application and Caldwell. Instant claims 3-6, 11, 15 and 17-19 depend from instant claim 2 and, thus, also are not obvious over the claims of the 049 application and Caldwell.

VIII. CONCLUSION

For the above reasons, it is respectfully requested that all outstanding rejections of the pending claims be REVERSED.

Respectfully submitted,

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Attachments:

Claims Appendix
Evidence Appendix
Related Proceedings Appendix
Dictionary Excerpt

CLAIMS APPENDIX

Claim 1 (Cancelled).

Claim 2 (Previously Presented): A method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface, said method comprising the steps:

- (i) providing a hydrophobic surface,
- (ii) immobilizing hydrophilic macromolecules on the hydrophobic surface,
- (iii) exposing the hydrophilic macromolecules immobilized on the hydrophobic surface to hydrophilic species, whereby the hydrophilic species are attached to the hydrophilic macromolecules.

Claim 3 (Previously Presented): A method according to claim 2, characterized in that the hydrophilic species comprises nanoparticles.

Claim 4 (Previously Presented): A method according to claim 2, characterized in that the hydrophilic species is in solution.

Claim 5 (Previously Presented): A method according to claim 2, comprising the additional step:

- (iv) growing the attached hydrophilic species to a larger size.

Claim 6 (Previously Presented): A method according to claim 5, characterized in that growing the attached hydrophilic species to a larger size is achieved by exposing the attached hydrophilic species to an electroless plating solution.

Claim 7 (Previously Presented): A method according to claim 2, characterized in that immobilizing the hydrophilic macromolecules on the hydrophobic surface occurs by applying the hydrophilic macromolecules to the hydrophobic surface.

Claim 8 (Previously Presented): A method according to claim 7, characterized in that applying the hydrophilic macromolecules to the hydrophobic surface occurs by a process selected from spin-coating, dip-coating, drop-casting, stamping, molecular combing, spraying-techniques, inkjet-printing and doctor-blading.

Claim 9 (Previously Presented): A method according to claim 2, characterized in that exposing the hydrophilic macromolecules to hydrophilic species, whereby the hydrophilic species are attached to the hydrophilic macromolecules, occurs over a period of time between 1 second and 120 minutes.

Claim 10 (Previously Presented): A method according to claim 9, characterized in that exposing the hydrophilic macromolecules to hydrophilic species occurs over a period of time between 10 seconds and 10 minutes.

Claim 11 (Previously Presented): A method according to claim 4, characterized in that the solution is a solution of the hydrophilic species in water or of the hydrophilic species in a water-miscible organic solvent/water mixture.

Claim 12 (Previously Presented): A method according to claim 2, characterized in that water has a contact angle on the hydrophobic surface in the range of from 30° to 110°.

Claim 13 (Previously Presented): A method according to claim 12, characterized in that water has a contact angle on the hydrophobic surface in the range of from 60° to 110°.

Claim 14 (Previously Presented): A method according to claim 2, characterized in that the hydrophilic species is selected from the group comprising water soluble metal nanoparticles,

semiconductor nanoparticles and dielectric (insulator) nanoparticles, hydrophilic clusters and metallic complexes.

Claim 15 (Previously Presented): A method according to claim 3, characterized in that the nanoparticle has a core and comprises a metal or metal oxide in the core, where the metal is selected from the group comprising Fe, Co, Ni, Cu, Ru, Rh, Pd, Os, Ir, Ag, Pt, Au or combinations, especially alloys of these metals.

Claim 16 (Previously Presented): A method according to claim 2, characterized in that the hydrophilic macromolecules are selected from the group comprising nucleic acids, proteins, dendrimers, latex spheres, polyelectrolytes, and water-soluble polymers.

Claim 17 (Previously Presented): A method according to claim 16, characterized in that the nucleic acid is selected from the group comprising DNA, RNA, PNA, CNA, oligonucleotides, oligonucleotides of RNA, A-DNA, B-DNA, Z-DNA, polynucleotides of DNA, polynucleotides of RNA, T-junctions of nucleic acids, triplexes of nucleic acid, quadruplexes of nucleic acids, domains of non-nucleic acid polymer-nucleic acid block-copolymers and combinations thereof.

Claim 18 (Previously Presented): A method according to claim 17, characterized in that the nucleic acid is double-stranded or single-stranded.

Claim 19 (Previously Presented): A method according to claim 2, characterized in that the hydrophilic species is selected from the group comprising tris(hydroxymethyl)phosphine-gold nanoparticles (THPAuNPs).

Claim 20 (Previously Presented): A method according to claim 6, characterized in that the electroless plating solution comprises a gold salt and a reducing agent.

Claim 21 (Cancelled).

Claim 22 (Cancelled).

Claim 23 (Cancelled).

EVIDENCE APPENDIX

None.

RELATED PROCEEDINGS APPENDIX

None.



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